

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method for synthesising a bifunctional complex comprising an encoded molecule and an identifier polynucleotide identifying the chemical entities having participated in the synthesis of the encoded molecule, said method comprising the steps of

providing

- a) at least one template comprising one or more codons capable of hybridising to an anti-codon, wherein said template is optionally associated with one or more chemical entities, and
- b) a plurality of building blocks each comprising an anti-codon associated with one or more chemical entities, and

hybridising the anti-codon of one or more of the provided building blocks to the template,

covalently linking said anti-codons and/or linking the at least one template with the anti-codon of at least one building block, thereby generating an identifier polynucleotide capable of identifying chemical

entities having participated in the synthesis of the encoded molecule,

separating the template from one or more of the anti-codons hybridised thereto, thereby generating an at least partly single stranded identifier polynucleotide associated with a plurality of chemical entities,

generating a bifunctional complex comprising an encoded molecule and an identifier polynucleotide identifying the chemical entities having participated in the synthesis of the encoded molecule,

wherein said encoded molecule is generated by reacting at least two of said plurality of chemical entities associated with the identifier polynucleotide,

wherein said at least two chemical entities are provided by separate building blocks.

Claims 2-6 (Cancelled)

7. (Currently Amended) The method of ~~any of claims 1 to 6~~ claim 1, wherein the template is separated from said covalently linked anti-codons by chemically or enzymatically cleaving one or more nucleotide linking bonds of the template.

Claim 8 (Cancelled)

9. (Currently Amended) The method of ~~claim 8~~ 1, wherein the template is separated from said covalently

linked anti-codons in a separation step selected from the group consisting of i) a step involving heating the template and the covalently linked anti-codons, thereby displacing the template from the covalently linked anti-codons, and ii) a step involving washing the template and the covalently linked anti-codons in a solvent resulting in displacing the template from the covalently linked anti-codons, wherein said steps are optionally followed by one or more washing steps.

10. (Currently Amended) The method of ~~any of claims 1 to 9~~ claim 1, wherein at least one of said covalently linked anti-codons is further linked to a solid support, wherein the template is hybridised to the covalently linked anti-codons without being covalently linked to said covalently linked anti-codons, and wherein the template is separated from the covalently linked anti-codons by a step involving heating the template and the covalently linked anti-codons and/or a washing step resulting in physically separating the template from the covalently linked anti-codons.

Claim 11 (Cancelled)

12. (Currently Amended) The method of ~~any of claims 1 to 9~~ claim 1, wherein the template is linked to a solid support, wherein said covalently linked anti-codons are hybridised to the template without being covalently linked to said template, and wherein the covalently linked anti-codons are separated from the template by a step involving heating the template and the covalently linked anti-codons and/or a washing step resulting in physically

separating the covalently linked anti-codons from the at least one template.

13. (Original) The method of claim 12, wherein at least one of said covalently linked anti-codons are further linked to one member of an affinity pair, wherein the other member of said affinity pair is linked to a further solid support, wherein the linkage of said affinity pair members results in attaching said covalently linked anti-codons to said further support.

14. (Currently Amended) The method of ~~any of claims 7 to 13~~ claim 7, wherein the identifier polynucleotide consists of covalently linked anti-codons.

15. (Currently Amended) The method of ~~any of claims 7 to 13~~ claim 7, wherein the identifier polynucleotide does not comprise the template, or a part thereof.

Claims 16-21 (Cancelled)

22. (Original) The method of claim 1,

wherein the anti-codon of one of the provided building blocks is hybridised to the template,

wherein the anti-codon is covalently linked to the template,

wherein the anti-codon is displaced from the template, thereby generating an at least essentially single

stranded identifier polynucleotide associated with a plurality of chemical entities,

wherein at least two of said plurality of chemical entities associated with the at least essentially single stranded identifier polynucleotide are reacted, thereby generating a bifunctional complex comprising a first encoded molecule and an identifier polynucleotide coding for chemical entities having participated in the synthesis of the first encoded molecule.

23. (Original) The method of claim 22 comprising the further steps of

i) hybridising the anti-codon of at least one further building block to the identifier polynucleotide of the first bifunctional complex ~~generated in claim 7~~, wherein said anti-codon is associated with one or more chemical entities,

ii) covalently linking the anti-codon and the identifier polynucleotide of the first bifunctional complex,

iii) displacing the anti-codon from the identifier polynucleotide of the first bifunctional complex, thereby generating an at least essentially single stranded second identifier polynucleotide associated with the first encoded molecule and one or more chemical entities,

iv) reacting the first encoded molecule and the one or more chemical entities, and

v) generating a second bifunctional complex comprising a second encoded molecule and the second identifier oligonucleotide identifying the plurality of chemical entities having participated in the synthesis of the second encoded molecule.

24. (Original) The method of claim 23, wherein steps i) to iv) are repeated for building blocks comprising different anti-codons and/or different chemical entities, thereby generating a plurality of bifunctional complexes comprising different encoded molecules.

Claim 25 (Cancelled)

26. (Currently Amended) The method of ~~any of claims 1 to 25~~ claim 1, wherein the template comprises from 2 to preferably less than 100 codons, such as from 2 to preferably less than 10 codons.

Claims 27-28 (Cancelled)

29. (Currently Amended) The method of ~~any of claims 1 to 28~~ claim 1, wherein each codon comprises from 3 to 30 nucleotides.

Claims 30-37 (Cancelled)

38. (Currently Amended) The method of ~~any of claims 1 to 37~~ claim 1, wherein at least one of said building blocks comprise a chemical entity comprising a scaffold moiety comprising a plurality of reactive groups, and/or wherein the template is linked to a chemical entity

comprising a scaffold moiety comprising a plurality of reactive groups.

39. (Original) The method of claim 38, wherein said scaffold moiety reactive groups react with one or more chemical entities of a single building block, or one or more chemical entities of different building blocks.

Claims 40-56 (Cancelled)

57. (Currently Amended) The method of ~~any of claims 1 to 56~~ claim 1, wherein at least one building block or a subset of said plurality of building blocks are provided sequentially and/or sequentially hybridised to the template, wherein said sequentially provided and/or hybridised building block anti-codons are ligated, and wherein chemical entities of said subset of sequentially provided building blocks react before a further subset of building blocks are provided and/or hybridised to the template.

Claims 58-67 (Cancelled)

68. (Currently Amended) The method of ~~any of claims 1 to 65~~ claim 1, wherein at least some building block anti-codons are ligated to the anti-codon of a neighbouring building block and/or to a template by a ligase, thereby covalently linking said building block anti-codons.

Claims 69-70 (Cancelled)

71. (Currently Amended) The method of ~~any of the preceding claims~~ claim 1, wherein the at least essentially single stranded identifier polynucleotide is obtained by displacing codons and anti-codons under denaturing conditions resulting in said displacement.

Claims 72-73 (Cancelled)

74. (Original) The method of claim 7 comprising the further step of degrading the template part of the identifier polynucleotide before any of the chemical entities are reacted.

Claims 75-77 (Cancelled)

78. (Currently Amended) The method of ~~any of claims 1 to 77~~ claim 1 comprising the further step of separating the template from a plurality of covalently linked anti-codons before reacting any chemical entities, reacting the chemical entities and generating a bifunctional complex comprising an encoded molecule and an identifier oligonucleotide consisting solely of ligated anti-codons, wherein said identifier oligonucleotide identifies the chemical entities having participated in the synthesis of the encoded molecule.

79. (Original) The method of claim 78, wherein the template is removed by cleaving at least one covalent link linking template codons and building block anti-codons, subjecting to cleavage product to conditions eliminating hybridisation between template codons and building block anti-codons, and separating the template from the covalently linked anti-codons.

80. (Original) The method of claim 79, wherein the covalent link is cleaved by a restriction endonuclease.

Claims 81-83 (Cancelled)

84. (Currently Amended) The method of ~~any of~~
~~claims 1 to 83~~ claim 1 comprising the further step of separating codons and anti-codons by hybridising a nucleic acid to the template part of the molecule, thereby generating a duplex comprising the template.

Claims 85-90 (Cancelled)

91. (Currently Amended) The method of ~~any of the~~
~~preceding claims~~ claim 1, wherein a plurality of bifunctional complexes are generated from the hybridisation of a plurality of templates to a plurality of building block anti-codons, covalently linking anti-codons hybridised to the same template, separating the template from at least some of the covalently linked anti-codons, preferably by degrading the template or by cleaving at least one chemical bond linking the template to the covalently ligated anti-codons followed by physical separation of the template and the covalently linked anti-codons, reacting the chemical entities and generating a library of bifunctional complexes each comprising a different encoded molecule and an identifier polynucleotide identifying the chemical entities having participated in the synthesis of the encoded molecule, wherein each of the plurality of encoded molecules are

generated by reacting chemical entities associated with different anti-codons.

Claims 92-120 (Cancelled)

121. (Original) The method of claim 1,

wherein the anti-codons of from 3 to 8 building blocks are hybridised to a template sequentially or simultaneously in the same first compartment,

wherein at least one of the building blocks comprise a scaffold moiety comprising a plurality of reactive groups associated to an anti-codon,

wherein the template is covalently bound to a solid support, such as a beaded polymer,

wherein the covalently linked anti-codons are separated from the template covalently bound to the solid support, wherein said separation results in anti-codons and codons not being hybridised to each other,

optionally transferring the covalently ligated anti-codons to a second compartment, or transferring the template covalently bound to a solid support to a second compartment, and

reacting the chemical entities associated with the identifier polynucleotide, optionally in a compartment different from the compartment harbouring the template.

122. (Original) The method of claim 1,

wherein the anti-codons of from 3 to 8 building blocks are hybridised to a template sequentially or simultaneously in the same first compartment,

wherein at least one of the building blocks comprise a scaffold moiety comprising a plurality of reactive groups associated with an anti-codon,

wherein the covalently linked anti-codons are initially covalently linked to the template,

wherein the template part of the identifier oligonucleotide is degraded, thereby generating an identifier oligonucleotide comprising an essentially single stranded molecule comprising no template sequence,

optionally transferring the covalently ligated anti-codons to a second compartment, and

reacting the chemical entities associated with the identifier polynucleotide.

123. (Original) The method of claim 122, wherein the building blocks are provided sequentially, and wherein said method comprises the further steps of

- i. covalently linking the anti-codon of a sequentially added building block to the template, or covalently linking the anti-codon of a sequentially added building block to an anti-codon covalently linked to the template,

- ii. selecting a set of reaction conditions wherein codons and anti-codons do not hybridise to each other, thereby generating an essentially single stranded molecule,
- iii. reacting a chemical entity of a sequentially added building block with a chemical entity associated with the template, or with a chemical entity associated with an anti-codon covalently linked to the template, and
- iv. repeating steps i) to iii) for different building blocks.

124. (Original) A method for synthesising one or more bifunctional complexes each comprising a molecule resulting from the reaction of a plurality of chemical entities and an identifier polynucleotide identifying one or more of the chemical entities having participated in the synthesis of the molecule, said method comprising the steps of

- i. providing a plurality of building blocks each comprising an oligonucleotide associated with one or more chemical entities,
- ii. providing at least one connector oligonucleotide capable of hybridising with one or more building block oligonucleotides,
- iii. immobilising at least one building block to a solid support,

- iv. hybridising said immobilized building block oligonucleotide to a first connector oligonucleotide,
- v. hybridising at least one additional building block oligonucleotide to said first connector oligonucleotide,
- vi. ligating building block oligonucleotides hybridised to the connector oligonucleotide,
- vii. separating the connector polynucleotide from the ligated building block oligonucleotides,
- viii. reacting one or more chemical entities associated with different building block oligonucleotides, thereby obtaining a first bifunctional complex comprising a first molecule or first molecule precursor linked to a first identifier oligonucleotide identifying the chemical entities having participated in the synthesis of the molecule or molecule precursor, wherein said first bifunctional complex is immobilised to a solid support.

Claim 125 (Cancelled)

126. (Original) The method of claim 124 comprising the further steps of

- i. providing a second connector polynucleotide,

- ii. hybridising said second connector polynucleotide to the identifier polynucleotide of said first bifunctional complex,
- iii. hybridising at least one further oligonucleotide of a building block to said second connector oligonucleotide,
- iv. ligating building block oligonucleotides hybridised to the second connector oligonucleotide, wherein at least one of said building block oligonucleotides are hybridised to the first identifier polynucleotide,
- v. separating the second connector polynucleotide from the ligated building block oligonucleotides, for example by diverting the second connector polynucleotide to another compartment,
- vi. reacting the first molecule precursor with the one or more chemical entities associated with the ligated building block oligonucleotide(s), thereby obtaining a second bifunctional complex comprising a molecule or molecule precursor linked to a second identifier polynucleotide identifying the chemical entities having participated in the synthesis of the molecule or molecule precursor, wherein said second bifunctional complex is immobilised to a solid support.

Claims 127-129 (Cancelled)

130. (Original) A method for synthesising a bifunctional complex comprising a molecule resulting from the reaction of a plurality of chemical entities, wherein said molecule is linked to an identifier polynucleotide identifying one or more of the chemical entities having participated in the synthesis of the molecule, said method comprising the steps of

- i) providing a plurality of building blocks selected from the group consisting of
 - a) building blocks comprising an identifier oligonucleotide linked to one or more chemical entities,
 - b) building blocks comprising an identifier oligonucleotide linked to one or more reactive groups, and
 - c) building blocks comprising an identifier oligonucleotide comprising a spacer region, wherein said building blocks comprising a spacer region are preferably connector polynucleotides to which building blocks of groups a) and b) can hybridise,
- ii) generating a hybridisation complex comprising at least n building blocks by hybridising the identifier oligonucleotide of one building block to the identifier oligonucleotide of at least one other building block,

wherein n is an integer of 4 or more

wherein at least 3 of said at least n building blocks comprise a chemical entity,

wherein no single identifier oligonucleotide is hybridised to all of the remaining identifier oligonucleotides,

wherein optionally at least one of said building blocks of group c) is immobilised to a solid support, thereby providing a handle to which an oligonucleotide of at least one building block of groups a) or b) can hybridise,

- iii) covalently linking identifier oligonucleotides of building blocks comprising one or more chemical entities, thereby obtaining an identifier polynucleotide comprising covalently linked identifier oligonucleotides each associated with one or more chemical entities,
- iv) optionally separating said identifier polynucleotide obtained in step iv) from any immobilised connector oligonucleotides hybridised thereto, wherein said separation optionally comprises the step of diverting said identifier polynucleotide comprising covalently linked identifier oligonucleotides each associated with one or more chemical entities to a different reaction compartment, thereby separating said identifier polynucleotide from said immobilised connector oligonucleotides

- v) reacting said at least 3 chemical entities linked to the identifier polynucleotide, and
- vi) obtaining a bifunctional complex comprising a molecule resulting from the reaction of a plurality of chemical entities, wherein said molecule is linked to an identifier polynucleotide identifying one or more of the chemical entities having participated in the synthesis of the molecule.

131. (Original) The method of claim 130 wherein a plurality of different bifunctional complexes is obtained by repeating the method steps for different building blocks.

Claims 132-205 (Cancelled)